CDER Draft Guidance Document Release Form

Title of Document: Guidance for Industry: Submitting Application Archival Copies in Electronic Format

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Originating Organization (Office, Division, Coordinating Committee):

Release Requested for:

__X_ Workshop Discussion (Date of Workshop: November 6-7, 1996)

____ Federal Register

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Guidance for Industry

SUBMITTING APPLICATION ARCHIVAL COPIES IN ELECTRONIC FORMAT

DRAFT GUIDANCE - NOT FOR IMPLEMENTATION

This guidance document is being distributed for comment purposes only.

Draft released for comment on: November 4, 1996.

Comments and suggestions regarding this draft document should be submitted by December 31, 1996. Comments and suggestions received after this date may not be acted upon by the Agency until the document is next revised or updated. For CDER questions regarding this draft document, contact Gregory Brolund, HFD-072, 5600 Fishers Lane, Rockville, MD 20857 (301-827-3276). For CBER questions, contact Mary Buesing, HFM-124, 1401 Rockville Pike, Rockville, MD 20852 (301-827-3726); or via E-mail at archiv@A1.cber.fda.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
October 1996

IT #xx

Table of Contents

DRAFT — Not for implementation

GUIDANCE FOR INDUSTRY[1]

SUBMITTING APPLICATION ARCHIVAL COPIES IN ELECTRONIC FORMAT

I. INTRODUCTION

Currently, FDA requires by regulation that a variety of drug regulatory submissions be filed as paper documents. For example, regulations in 21 CFR Part 314 describe the procedures and requirements for submitting applications for FDA approval to market new drugs to the Center for Drug Evaluation and Research (CDER). These regulations require the submission of three paper copies of an application for marketing approval: (1) a complete archival copy, (2) a review copy, and (3) a field copy [21 CFR 314.50(k)]. In the Center for Biologics Evaluation and Research (CBER), the policy for product license applications (PLA) and biologics license applications (BLA) has been to receive an original and two copies. However, a proposed regulation, Electronic Signatures and Records, 21 CFR Part 11, would permit the submission of an application or parts of an application, including archival copies, in electronic format without an accompanying paper copy.

Proposed 21 CFR Part 11 provides for the Agency to establish a docket on electronic submissions in which the Agency will notify the public when it is ready to accept specific types of electronic submissions. The docket will describe those submissions that may be made in electronic form in whole or in part and identify the corresponding Agency units ready to receive these submissions. The docket will also contain technical guidance on how to make those submissions, depending on the receiving unit's capabilities. The Agency expects to

[1]This guidance has been prepared by the Information Technology Coordinating Committee (ITCC) in the Center for Drug Evaluation and Research (CDER) and representatives from the Information Technology Implementation Committee (ITIC) and Document Control Center (DCC) in the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration. Although this guidance does not create or confer any rights for or on any person and does not operate to bind FDA or the industry, it does represent the Agency's current thinking on submitting archival copies of applications in electronic format. For additional copies of this guidance access the document on the WWW, connect to the CDER Home Page at http://www.fda.gov/cder and go to the "Regulatory Guidance" section. The CBER WWW site address is http:/www.fda.gov/cberftp.html. A copy of the document may also be obtained via FAX by calling CBER at 1-800-cber-fax or via "bounce-back" e-mail by sending a message to earc@Al.cber.fda.gov.

publish a final regulation soon, and it will take effect five months after final publication.

Once the regulation takes effect and technical guidance is in the docket for a specific type of document, CDER will have the ability to begin accepting electronic submissions, including documents submitted under investigational new drug applications (IND), new drug applications (NDA), abbreviated new drug applications (ANDA), and abbreviated antibiotic drug applications (AADA). CBER similarly will have the ability to begin accepting electronic submissions of an IND, NDA, biologic or product license application (BLA or PLA), an investigational device exemption (IDE), premarket application (PMA), and premarket notification (510k). However, because it will be impossible to move from paper to electronic format all at once, the Agency is proposing to move from paper regulatory submissions to electronic regulatory submissions in stages. The exact approach is presently under development. The Agency hopes that such an approach will allow the Agency to avoid disruptions to the review process while keeping costs to a minimum.

To facilitate the efficient handling and continued access to all electronic archival submissions under the proposed regulation, CDER and CBER are developing a standard policy on the format of such archival copies. To ensure that electronic information will be legible and printable indefinitely, electronic submissions of the archival copy should be made using the standard archival format described in this guidance and the specifications described in the document type's technical guidance. Currently, other electronic submissions also may include additional customized, proprietary formats as part of the **review copy** of the document. However, these submissions may not be acceptable as the electronic archival copy.

This guidance represents the Agency's first attempt to develop a format for preparing electronic archival submissions. As with other guidance documents, FDA does not intend this guidance document to be all-inclusive and cautions that not all information may be applicable to all situations. The guidance document is intended to provide information and does not set forth requirements. The methods and procedures cited in the guidance are suggestions. FDA anticipates that sponsors and investigators may develop alternative methods and procedures and discuss them with the Agency, and the FDA may find those alternative methods and procedures acceptable. Because this is a rapidly developing field, this guidance most likely will be updated periodically.

II. DEFINITION OF ELECTRONIC SUBMISSION

An electronic submission may contain the following components.

- Text and tables in a word processor format
- Images (e.g., case report forms)
- Programs, macros, and procedures for retrieval and data analysis
- Datasets for study reporting and statistical analysis
- Electronic signatures

An electronic submission may use a combination of software tools and data formats that are integrated into a system intended to achieve the maximum efficiency in submission review.

III. TEXT AND IMAGES

The major goals of text and image archives are twofold: (1) Provide an exact replica of each page as it would have been printed in a paper submission (i.e., retaining fonts, special orientations, and page numbering). (2) Allow the viewer to navigate through the electronic document using at least the standard table of contents currently provided with paper copy submissions.

To accomplish these goals, text and image pages should be submitted in Adobe Portable Document Format (PDF)[2] and should retain the appearance of the original text when displayed and printed. All PDF archival submissions should contain a master document with hypertext links that serve as the table of contents for the submission. The table of contents should link directly to the correct electronic volume needed to display the text, image, table, analysis, or case report form.

Sponsors should also include the following in any PDF submission:

- A written description of any navigational strategy used creating the PDF archive: PDF hyperlink, PDF bookmarks, PDF thumbnails, PDF annotation, any indexing provided by the sponsor.

- Documentation of the methods and tools used to create the PDF files.

- Documentation of the word processor or other software used to produce the PDF files in the electronic submission.

[2]FDA use of specific products does not constitute an endorsement of that product.

- Documentation of the file and directory naming convention and relationships between the PDF files and the information provided in any hard copies (e.g., EVOL01.PDF = Efficacy Summary Volume 1, SAFREPZ.PDF = Safety Report for Study Z).

The sponsor may wish to consult with the review division regarding the development of a review copy of the electronic submission that can contain customized methods for searching and analyzing data in a submission. This review copy is different from the archival copy in that it includes features that might make it impossible to access the information in the future. (Viewing or printing the archival copy of a submission should not depend on a non-PDF navigational feature external to the PDF files.)

Prior to submission of an archival or customized review copy, the sponsor or applicant should consult with the Division of Information Systems Design (CDER) or the Division of Applied Information Technology (CBER) to ensure that the file and directory naming conventions for the application are compatible with the Agency's systems and network.

IV. PROGRAMS AND MACROS

Any programs or macros necessary to display, retrieve, or analyze data should be fully described in a document submitted in PDF format so that the information can be reproduced in a system of CDER's choice.

Submisions to CBER also should include the original programs and macros. For example, if SAS datasets are included, then the programs and macros also should be provided for generating the sponsor's analysis.

V. DATASETS

In addition to the PDF files for the text, printed tables, and images, all datasets intended for use in further analyses should be in ASCII and include a detailed data definition. The data definition, which should be submitted as a PDF or ASCII text document, should generally include the record and field descriptions (including data types and locations) as well as a narrative definition of each field. The data definition should be sufficient to allow the Agency to accurately load the data into a database or analysis system of the Agency's choice.

Submission to CBER should include an archival copy of the original analysis dataset (e.g., SAS, SPLUS, etc.) in addition to the ASCII data.

VI. MEDIA

Electronic information should be submitted to CDER's Central Document Room on either magnetic tape or CD-ROM; electronic submissions to CBER should go to CBER's Document Control Center. Both CDER and CBER currently support ISO 9660 CD-ROM. In addition, CDER will provide specific magnetic tape specifications to each sponsor prior to submission of the application. (CDER supports 8 mm tape, 4 mm DAT tape in ASCII format or in Digital Equipment Corporation OpenVMS backup format.)